aCGH Deletion/ Duplication Analysis

Versiti's custom designed, high density gene-focused array allows for the detection of small deletions and duplications within a single exon of a given gene and large deletions and duplications encompassing one or more exons, or the entire gene.

Large deletions and duplications, also referred to as copy number variation (CNV), are a known cause of genetic disorders, but can escape detection by standard sequence analysis. Depending on the gene of interest, deletions and duplications have been shown to be responsible for approximately 10% of genetic disease. Array Comparative Genomic Hybridization (aCGH) has proven to be a highly sensitive and accurate tool in detection of these deletions and duplications. High resolution aCGH complements DNA sequencing and provides comprehensive mutation analysis.

Indications for testing:

- Patients with hematologic disorders with a possible genetic etiology mainly caused by deletions/ duplications.
- Patients with hematologic disorders with a possible genetic etiology where no pathogenic variant or a single variant for recessive disease has been identified by DNA sequencing.
- Patients with prior DNA sequence analysis in which amplification of one or more exons failed.

Test method:

The specific genes are analyzed for copy number variation due to deletion or duplication by high density gene-focused array Comparative Genomic Hybridization. Probes are approximately 60 bp in length, and density of coverage in exonic regions is approximately 4 probes per 500 bp. Genomic DNA for the samples and gender-matched references are denatured, labeled with fluorescent dye and hybridized. The array is washed and scanned. Data is returned and analysis is performed for the specific genes requested.

Assay sensitivity and limitations:

Balanced chromosomal rearrangements (i.e., translocations, inversions) or point mutations that may be the cause of the clinical phenotype cannot be detected via this method. Some small exonic deletions or duplications, or those present at low levels of mosaicism, may not be detected. Intronic regions have varying degrees of coverage. Probe performance could be affected by multiple SNPs in a given region, or high GC content. Breakpoints, if occurring outside the targeted gene, may be difficult to define.

Reporting of results:

Reportable Range – Results are reported heterozygous, homozygous or hemizygous deletion/duplication.

Specimen requirements:

Fetal: 7-15ml Amniotic Fluid, Cultured Amniocytes ($2x10^6$ minimum), 5-10gm CVS or Two T25 flasks Cultured CVS.

Parental/Patient: 3-5 ml EDTA (lavender top) whole blood.

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SHIP

Shipping requirements:

Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address package to:

Versiti Client Services
Molecular Diagnostics Laboratory
638 N. 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

ORDER

Required forms:

Please complete all pages of the requisition form. Clinical history (including patient's ethnicity, clinical diagnosis, family history and relevant laboratory findings) is necessary for optimal interpretation of genetic test results and recommendations. Clinical and laboratory history can either be recorded on the requisition form or clinical and laboratory reports can be submitted with the sample.

CPT Codes/Billing/Turnaround time:

Test code: 4800

CPT codes: F8: 81406, VPS13B: 81407

All Other Genes: 81479

Turnaround time: 21 days

References:

1. Askree S, Chin E, Bean L, Coffee B, Tanner A, Hegde M: Detection limit of intragenic deletions with targeted array comparative genomic hybridization. BMC Genetics 2013, 14:116 doi:10.1186/1471-2156-14-116
2. Curtis C, Lynch A, Dunning M, Spiteri I, Marioni J, Hadfield J, Chin S, Brenton J, Tavaré S, Caldas C: The pitfalls of platform comparison: DNA copy number array technologies assessed. BMC Genomics 2009, 10:588 doi: 10.1186/1471-2164-10-588
3. Xue Y, Ankala A, Wilcox WR, Hegde MR: Solving the molecular diagnostic testing conundrum for Mendelian disorders in the era of next-generation sequencing: single-gene, gene panel, or exome/genome sequencing. Genet Med. 2015 Jun;17(6):444-451. doi: 10.1038/gim.2014.122. Epub 2014 Sep 18.

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